

Appl. No. : 09/893,244  
Filed : June 27, 2001

### REMARKS

Claims 85-88 are pending in the application. Reconsideration and withdrawal of the present rejection in view of the comments presented herein are respectfully requested.

#### Discussion of Rejection under 35 U.S.C. § 103 – Obviousness

The Examiner rejects Claims 85-88 under 35 U.S.C. § 103(a) as being unpatentable over Lidsky (US Patent No. 5,602,150) in view of Vetulani (Review Drug Addiction. Part III. Pharmacotherapy of Addiction, *Polish Journal of Pharmacology*, 2001, Vol. 53, pp. 415-434), in view of Bormann et al. (US Patent No. 5,061,703) and further in view of Decollogne et al. (NMDA Receptor Complex Blockade by Oral Administration of Magnesium: Comparison with MK-801, 1997, *Pharmacology Biochemistry and Behavior*, Vol. 58, No. 1, pp. 261-268). The Examiner argues that it is *prima facie* obvious to combine two compositions (i.e., acamprosate and magnesium), each of which is taught to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.

The Examiner further asserts that the previously submitted Rule 132 Declaration provided with Applicant's response dated October 27, 2006 was insufficient to overcome the rejections of record because the declaration allegedly does not demonstrate synergism of acamprosate and magnesium. In particular, the Examiner argues that in the Declaration, the dosage of magnesium given with acamprosate is allegedly higher than the dose given when magnesium was administered alone. In support of this argument, the Examiner alleges that chelated minerals are more readily absorbed in the digestive tract than non-chelated forms.

A *prima facie* case of obviousness cannot be maintained if a combination has unexpected results such as a synergistic effect. M.P.E.P. 716.02(a). "Evidence rising out of the so-called 'secondary considerations' must always when present be considered en route to a determination of obviousness." See *Stratoflex Inc. v. Aeroquip Corp.*, 713 F.2d 1530, 1538 (Fed. Cir. 1983).

Applicant maintains that the combination of acamprosate and magnesium has synergistic effects. In support of the secondary considerations, Applicant submits herewith new Rule 132 Declaration of Barry S. Fogel, M.D. Here, secondary considerations, specifically unexpected results, are demonstrated by the newly submitted Rule 132 Declaration of Barry S. Fogel, M.D.

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This objective evidence of unexpected results demonstrates that the instant claims are not obvious.

As demonstrated by the instant Declaration of Barry S. Fogel, M.D., the combination of acamprosate and magnesium was significantly better at alleviating tardive dyskinesia (TD) symptoms than was acamprosate alone. Importantly, the administration of magnesium alone had no effect in alleviating such symptoms (Declaration at paragraphs 4 and 5). In particular, when the patient described in the declaration was administered magnesium alone, no improvement in symptoms was observed (Declaration at paragraph 5). Since magnesium alone had no beneficial therapeutic effect, it would be expected that the combination of magnesium and acamprosate would result in no additional therapeutic efficacy compared to acamprosate alone. However, when the patient described in the declaration was administered magnesium and acamprosate, the combination resulted in a greater than additive (i.e., synergistic) effect because significant improvements in symptoms were observed compared to acamprosate alone. This would not have been expected based on the lack of therapeutic efficacy of magnesium. The combination of acamprosate and magnesium also resulted in significant improvements compared to acamprosate alone (Declaration at paragraph 6). In view of the lack of therapeutic efficacy of magnesium alone, these results also demonstrate the synergistic effect of acamprosate and magnesium.

The Declaration also states that when magnesium was administered alone, the dosage was an equivalent of 300 mg elemental magnesium three times daily. The dosage administered in the combination therapy was at a dosage equivalent to 250 mg elemental magnesium three times daily. Accordingly, one would not expect that a lower dose of magnesium would have any greater effect than the higher dose.

Thus, the case studies and Declaration provide objective evidence of non-obviousness because they demonstrate unexpected results from the combination of acamprosate with magnesium. Specifically, they demonstrate synergy in improvement of symptoms associated with movement disorders such as TD.

For the above reasons, Applicant submits that Claims 85-88 are not obvious over the cited references. Thus, reconsideration and withdrawal of the rejection under 35 U.S.C. § 103 are respectfully requested.

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Conclusion

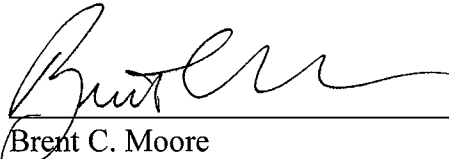
Applicant has endeavored to address all of the Examiner's concerns as expressed in the outstanding Office Action. In view of the above amendments and remarks, the present application is believed to be in condition for allowance, and action to that effect is respectfully solicited. Applicant invites the Examiner to call the undersigned if any issues may be resolved by telephone.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

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